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10/590,938	01/09/2007	Catharina Svanborg	BJS-4984-7	2661

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EXAMINER	
DESAI, ANAND U	
ART UNIT	PAPER NUMBER
1656	
MAIL DATE	DELIVERY MODE
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Please find below and/or attached an Office communication concerning this application or proceeding.

The time period for reply, if any, is set in the attached communication.

Office Action Summary	Application No.	Applicant(s)	
	10/590,938	SVANBORG, CATHARINA	
	Examiner	Art Unit	
	ANAND U. DESAI	1656	

-- The MAILING DATE of this communication appears on the cover sheet with the correspondence address --

Period for Reply

A SHORTENED STATUTORY PERIOD FOR REPLY IS SET TO EXPIRE 3 MONTH(S) OR THIRTY (30) DAYS, WHICHEVER IS LONGER, FROM THE MAILING DATE OF THIS COMMUNICATION.

- Extensions of time may be available under the provisions of 37 CFR 1.136(a). In no event, however, may a reply be timely filed after SIX (6) MONTHS from the mailing date of this communication.
- If NO period for reply is specified above, the maximum statutory period will apply and will expire SIX (6) MONTHS from the mailing date of this communication.
- Failure to reply within the set or extended period for reply will, by statute, cause the application to become ABANDONED (35 U.S.C. § 133). Any reply received by the Office later than three months after the mailing date of this communication, even if timely filed, may reduce any earned patent term adjustment. See 37 CFR 1.704(b).

Status

1)☒ Responsive to communication(s) filed on *26 June 2009*.

2a)☒ This action is **FINAL**. 2b)☐ This action is non-final.

3)☐ Since this application is in condition for allowance except for formal matters, prosecution as to the merits is closed in accordance with the practice under *Ex parte Quayle*, 1935 C.D. 11, 453 O.G. 213.

Disposition of Claims

4)☒ Claim(s) *22-28,38 and 40-50* is/are pending in the application.

4a) Of the above claim(s) _____ is/are withdrawn from consideration.

5)☐ Claim(s) _____ is/are allowed.

6)☒ Claim(s) *22-28,38 and 40-50* is/are rejected.

7)☐ Claim(s) _____ is/are objected to.

8)☐ Claim(s) _____ are subject to restriction and/or election requirement.

Application Papers

9)☐ The specification is objected to by the Examiner.

10)☐ The drawing(s) filed on _____ is/are: a)☐ accepted or b)☐ objected to by the Examiner.

Applicant may not request that any objection to the drawing(s) be held in abeyance. See 37 CFR 1.85(a).

Replacement drawing sheet(s) including the correction is required if the drawing(s) is objected to. See 37 CFR 1.121(d).

11)☐ The oath or declaration is objected to by the Examiner. Note the attached Office Action or form PTO-152.

Priority under 35 U.S.C. § 119

12)☐ Acknowledgment is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d) or (f).

a)☐ All b)☐ Some * c)☐ None of:

1.☐ Certified copies of the priority documents have been received.

2.☐ Certified copies of the priority documents have been received in Application No. _____.

3.☐ Copies of the certified copies of the priority documents have been received in this National Stage application from the International Bureau (PCT Rule 17.2(a)).

* See the attached detailed Office action for a list of the certified copies not received.

Attachment(s)

1) ☐ Notice of References Cited (PTO-892)
2) ☐ Notice of Draftsperson's Patent Drawing Review (PTO-948)
3) ☒ Information Disclosure Statement(s) (PTO/SB/08) Paper No(s)/Mail Date *20090629*.
4) ☐ Interview Summary (PTO-413) Paper No(s)/Mail Date. _____.
5) ☐ Notice of Informal Patent Application
6) ☐ Other: _____.

DETAILED ACTION

1. This office action is in response to the amendment filed on June 26, 2009. Claims 29-35 and 37 have been cancelled. New claims 40-50 have been added.

2. Claims 22-28, 38, and 40-50 are currently pending and under examination.

Information Disclosure Statement

3. The information disclosure statement (IDS) submitted on June 26, 2009 is being considered by the examiner. The signed 1449 form is attached with the office action.

Withdrawal of Rejections

4. The rejection of claims 22-28 and 38 under 35 U.S.C. 112, first paragraph, scope of enablement is withdrawn based on the remarks and the amendment to the claims drawn to enabled alpha-lactalbumin and cis C18:1:9 or cis C18:1:11 fatty acid cofactors.

5. The rejection of claims 22-28 and 38 under 35 U.S.C. 112, first paragraph, written description is withdrawn based on the remarks and the amendment to the claims drawn to described alpha-lactalbumin and cis C18:1:9 or cis C18:1:11 fatty acid cofactors.

Pending Rejections

Double Patenting

6. The nonstatutory double patenting rejection is based on a judicially created doctrine grounded in public policy (a policy reflected in the statute) so as to prevent the unjustified or improper timewise extension of the "right to exclude" granted by a patent and to prevent possible harassment by multiple assignees. A nonstatutory obviousness-type double patenting rejection is appropriate where the conflicting claims are not identical, but at least one examined application claim is not patentably distinct from the reference claim(s) because the examined

application claim is either anticipated by, or would have been obvious over, the reference claim(s). See, e.g., *In re Berg*, 140 F.3d 1428, 46 USPQ2d 1226 (Fed. Cir. 1998); *In re Goodman*, 11 F.3d 1046, 29 USPQ2d 2010 (Fed. Cir. 1993); *In re Longi*, 759 F.2d 887, 225 USPQ 645 (Fed. Cir. 1985); *In re Van Ornum*, 686 F.2d 937, 214 USPQ 761 (CCPA 1982); *In re Vogel*, 422 F.2d 438, 164 USPQ 619 (CCPA 1970); and *In re Thorington*, 418 F.2d 528, 163 USPQ 644 (CCPA 1969).

A timely filed terminal disclaimer in compliance with 37 CFR 1.321(c) or 1.321(d) may be used to overcome an actual or provisional rejection based on a nonstatutory double patenting ground provided the conflicting application or patent either is shown to be commonly owned with this application, or claims an invention made as a result of activities undertaken within the scope of a joint research agreement.

Effective January 1, 1994, a registered attorney or agent of record may sign a terminal disclaimer. A terminal disclaimer signed by the assignee must fully comply with 37 CFR 3.73(b).

7. Claims 22-28, 38, and 40-50 are provisionally rejected on the ground of nonstatutory obviousness-type double patenting as being unpatentable over claims 1-16 of copending Application No. 11/829,499 (U.S. 2008/0167233 A1; IDS document). Although the conflicting claims are not identical, they are not patentably distinct from each other because the claims are of overlapping scope. The claims of the copending application are drawn to a method of treating papilloma (proliferative disease) by administering to a patient in need thereof a biologically active complex of alpha-lactalbumin. The active complex of alpha-lactalbumin is known in the art as HAMLET once compelxed with a cis C18 unsaturated fatty acid cofactor.

This is a provisional obviousness-type double patenting rejection because the conflicting claims have not in fact been patented.

8. Claims 22 and 38 stand rejected, and newly submitted claims 40-42, and 44-50 are rejected on the ground of nonstatutory obviousness-type double patenting as being unpatentable over claims 1-16 of U.S. Patent No. 7,270,822 B2. Although the conflicting claims are not identical, they are not patentably distinct from each other because the claims are of overlapping

scope. The claims of the issued U.S. Patent are drawn to a method of treating papilloma (proliferative disease) by administering to a patient in need thereof a biologically active complex of alpha-lactalbumin. The active complex of alpha-lactalbumin is known in the art as HAMLET once compelxed with a cis C18 unsaturated fatty acid cofactor.

Response to Remarks

9. Applicant's state the obviousness-type double patenting rejection is obviated by the amendments to the claims. Applicant's arguments filed June 26, 2009 have been fully considered but they are not persuasive. The claims are of overlapping scope and are not patentably distinct from each other. The claims of the issued U.S. Patent are drawn to a method of treating papilloma (proliferative disease) by administering to a patient in need thereof a biologically active complex of alpha-lactalbumin. The active complex of alpha-lactalbumin is known in the art as HAMLET once compelxed with a cis C18 unsaturated fatty acid cofactor.

Claim Rejections - 35 USC § 112

10. The following is a quotation of the first paragraph of 35 U.S.C. 112:

> The specification shall contain a written description of the invention, and of the manner and process of making and using it, in such full, clear, concise, and exact terms as to enable any person skilled in the art to which it pertains, or with which it is most nearly connected, to make and use the same and shall set forth the best mode contemplated by the inventor of carrying out his invention.

11. Claims 46-50 are rejected under 35 U.S.C. 112, first paragraph, as failing to comply with the written description requirement. The claims contains subject matter, which was not described in the specification in such a way as to reasonably convey to one skilled in the relevant art that the inventors, at the time the application was filed, had possession of the claimed invention.

The response filed June 26, 2009 has introduced NEW MATTER into the claims. Newly added claims 46-50 recites that the cofactor is an unsaturated C16 to C18 fatty acid with a double bond in the cis configuration and including C18:2:9, 12 cis, C18:3,6, 9, 12 cis and C18:3:9, 12, 15 cis. The response did not point out where support for newly added claims could be found in the originally filed disclosure. Although the PTO has the initial burden of presenting evidence or reasons why persons skilled in the art would not recognize in the disclosure a description of the invention defined by the claims, when filing an amendment an applicant should show support in the original disclosure for new or amended claims. See MPEP 714.02 and 2163.06 ("Applicant should therefore specifically point out the support for any amendments made to the disclosure."). Instant claims now recites limitations, which were not clearly disclosed in the specification as filed, and now change the scope of the instant disclosure as filed. Such limitations recited in newly added claims, which did not appear in the specification, as filed, introduce new concepts and violate the description requirement of the first paragraph of 35 U.S.C 112. Applicant is required to provide sufficient written support for the limitations recited in present claims in the specification or claims, as-filed, or remove these limitations from the claims in response to this Office Action.

Furthermore, Applicant is referred to 37 CFR 1.57 (c) "Essential material" may be incorporated by reference, but only by way of an incorporation by reference to a **U.S. patent** or **U.S. patent application publication**, which patent or patent application publication does not itself incorporate such essential material by reference. "Essential material" is material that is necessary to: (1) Provide a written description of the claimed invention, and of the manner and process of making and using it, in such full, clear, concise, and exact terms as to

enable any person skilled in the art to which it pertains, or with which it is most nearly connected, to make and use the same, and set forth the best mode contemplated by the inventor of carrying out the invention as required by the first paragraph of 35 U.S.C. 112; (2) Describe the claimed invention in terms that particularly point out and distinctly claim the invention as required by the second paragraph of 35 U.S.C. 112; or (3) Describe the structure, material, or acts that correspond to a claimed means or step for performing a specified function as required by the sixth paragraph of 35 U.S.C. 112.

12. Claims 22-28, 38, and 40-45 are rejected under 35 U.S.C. 112, first paragraph, because the specification, while being enabling for a method for treating tumors in a patient comprising administering to a patient in need thereof, a biologically active complex of alpha-lactalbumin in the apo folding state (partially unfolded state), complexed with either cis C18:1:9 (oleic acid) or cis 18:1:11 (vaccenic acid), does not reasonably provide enablement for any biologically active complex comprising alpha-lactalbumin with any different fatty acid cofactor with a similar configuration to inhibit angiogenesis or treat any tumor. The specification does not enable any person skilled in the art to which it pertains, or with which it is most nearly connected, to make and use the invention commensurate in scope with these claims.

In *In re Wands*, 8 USPQ2d 1400 (Fed. Cir., 1988) eight factors are addressed in determining enablement.

The nature of the invention: the invention is drawn to a biologically active complex comprising alpha-lactalbuminfor the use in the treatment of mucosal tumors and/or to inhibit angiogenesis, wherein a cofactor which stabilizes the active complex includes a fatty acid with a similar configuration to cis C18:1:9 or cis C18:1:11.

The amount of direction or guidance presented:/The presence or absence of working examples: the example of using HAMLET generated on an C18:1:9 (oleic acid) conditioned ion-exchange chromatography column to isolate a complex which can be used treat tumors on patients do not in any way suggest that any cofactor would have the conformations necessary to be used in treating tumors or inhibit angiogenesis. The specification provides guidance with respect to the oleic acid discussed in the working example as the cofactor, but provides no guidance whatsoever in selecting which other cofactors might have the needed structure to stabilize the biologically active complex of alpha-lactalbumin. How does a different fatty acid have a similar configuration to cis C18:1:9 or cis C18:1:11 fatty acids? Does not the chemical make-up confer the structural arrangement of the molecules in the fatty acid cofactor? How is it a similar configuration?

3.) The predictability or unpredictability of the art: / 6.) The quantity of experimentation: there is predictability in the art with regard to the stereo-specific lipid-protein interactions required to form the biologically active complex of alpha-lactalbumin. Svensson et al. describe complexes of apo-alpha-lactalbumin with the cofactor of unsaturated C18 fatty acids in the cis configuration that have apoptotic activity on tumor cells. Svensson et al. state that saturated C18 fatty acids, unsaturated fatty acids in the trans configuration, or fatty acids with shorter carbon chains could not form the biologically active complex of alpha-lactalbumin (HAMLET) (see

Discussion, page 2810, 1st sentence on left column of text; previously cited). There is undue experimentation because of variability in prediction of apoptotic activity in the presence of different cofactors that can form biologically active complexes with HAMLET.

7.) The state of the prior art: the prior art has shown alpha-lactalbumin can alter its biological function depending on the conformational state. The conversion to HAMLET requires the partial unfolding of alpha-lactalbumin. The biological apoptotic activity requires the presence of C18:1 fatty acids (see 11/8/04 IDS document, Svensson et al., PNAS, Discussion, page 4225, paragraphs 1 through 3).

8.) Level of skill in the art: the level of skill in this art is high, at least that of a doctoral scientist with several years of experience in the art.

In consideration of each of factors discussed above, it is apparent that there is undue experimentation because of variability in prediction of outcome that is not addressed by the present application disclosure, examples, teaching, and guidance presented. Absent factual data to the contrary, the amount and level of experimentation needed is undue.

13. Claims 22-28, 38, and 40-45 are rejected under 35 U.S.C. 112, first paragraph, as containing subject matter which was not described in the specification in such a way as to reasonably convey to one skilled in the relevant art that the inventor(s), at the time the application was filed, had possession of the claimed invention. The instant claims are directed to a method of treating humans for mucosal tumors and/or inhibiting angiogenesis, which comprises administering to a patient a biologically active complex of alpha-lactalbumin

complexed with a cofactor that is a different fatty acid from cis C18:1:9 or cis C18:1:11 but with a similar configuration.

The Guidelines for Examination of Patent Applications Under the 35 U.S.C. 112, Paragraph 1, "Written Description" Requirement, published at Federal Register, Vol. 66, No. 4, pp. 1099-1111 outline the method of analysis of claims to determine whether adequate written description is present. The first step is to determine what the claim as a whole covers, i.e., discussion of the full scope of the claim. Second, the application should be fully reviewed to understand how applicant provides support for the claimed invention including each element and/or step, i.e., compare the scope of the claim with the scope of the description. Third, determine whether the applicant was in possession of the claimed invention as a whole at the time of filing. This should include the following considerations: (1) actual reduction to practice, (2) disclosure of drawings or structural chemical formulas, (3) sufficient relevant identifying characteristics such as complete structure, partial structure, physical and/or chemical properties and functional characteristics when coupled with a known or disclosed correlation between function and structure, (4) method of making the claimed invention, (5) level of skill and knowledge in the art and (6) predictability of the art. For each claim drawn to a single embodiment or species, each of these factors is to be considered with regard to that embodiment or species. For each claim drawn to a genus, each of these factors is to be considered to determine whether there is disclosure of a representative number of species that would lead one skilled in the art to conclude that applicant was in possession of the claimed invention. Where skill and knowledge in the art is high adequate written description would require fewer species to

be disclosed than in an art where little is known; further, more species would need to be disclosed to provide adequate written description for a highly variable genus.

First, what do the claims as a whole cover? Claims are directed to a method of treating mucosal tumors and/or inhibit angiogenesis using a biologically active complex of alpha-lactalbumin, comprising administering a biologically active complex of alpha-lactalbumin, which includes any cofactor, which stabilizes the complex in a biologically active form.

Second, how does the scope of the claims compare to the scope of the disclosure? The disclosure contains the same language found in claims and also discloses the specific complex comprising cis C18:1:9 fatty acid with the partially unfolded state of human alpha-lactalbumin. Thus, the specification is more detailed than claims.

Third, the factors need to be considered.

(1) What was actually reduced to practice?

The species comprising a partially unfolded state of human alpha-lactalbumin, complexed with cis C18:1:9 fatty acid is reduced to practice to treat tumors in patients in need thereof.

(2) Is there disclosure of drawings or structural chemical formulas?

There is no disclosure of how the alteration of alpha-lactalbumin results in a structure that gives rise to HAMLET activity in the presence of cis C18:1:9 fatty acid that is useful to treat tumors.

(3) Are there sufficient relevant identifying characteristics disclosed?

The specification provides guidance with respect to the oleic acid discussed in the working example as the cofactor, but provides no guidance whatsoever in

selecting which other cofactors might have the needed structure to stabilize the biologically active complex of alpha-lactalbumin. How does a different fatty acid have a similar configuration to cis C18:1:9 or cis C18:1:11 fatty acids? Does not the chemical make-up confer the structural arrangement of the molecules in the fatty acid cofactor? How is it a similar configuration?

(4) Is there at least one method of making the claimed invention disclosed?
One of skill in the art could easily produce the complex of human alpha-lactalbumin with cis C18:1:9 fatty acid as disclosed on page 10, lines 26-35, since only basic chromatography skills would be needed.

(5) What is the level of skill in the art and what knowledge is present in the art?
The level of skill in the art of protein pharmaceutical chemistry is high, about that of a PhD scientist with several years experience.

(6) What is the level of predictability of the art?
There is predictability in the art with regard to the stereo-specific lipid-protein interactions required to form HAMLET. Svensson et al. describe complexes of apo-alpha-lactalbumin with the cofactor of unsaturated C18 fatty acids in the cis configuration that have apoptotic activity on tumor cells. Svensson et al. state that saturated C18 fatty acids, unsaturated fatty acids in the trans configuration, or fatty acids with shorter carbon chains could not form HAMLET (see Discussion, page 2810, 1st sentence on left column of text).

Thus, having analyzed the claims with regard to the Written Description guidelines, it is clear that the specification does not disclose a representative number of species of different but

with similar configured fatty acids which would lead one skilled in the art to conclude that applicant was in possession of the claimed invention.

Conclusion

14. No claims are allowed.

15. Applicant's amendment necessitated the new ground(s) of rejection presented in this Office action. Accordingly, **THIS ACTION IS MADE FINAL**. See MPEP § 706.07(a). Applicant is reminded of the extension of time policy as set forth in 37 CFR 1.136(a).

A shortened statutory period for reply to this final action is set to expire THREE MONTHS from the mailing date of this action. In the event a first reply is filed within TWO MONTHS of the mailing date of this final action and the advisory action is not mailed until after the end of the THREE-MONTH shortened statutory period, then the shortened statutory period will expire on the date the advisory action is mailed, and any extension fee pursuant to 37 CFR 1.136(a) will be calculated from the mailing date of the advisory action. In no event, however, will the statutory period for reply expire later than SIX MONTHS from the date of this final action.

Any inquiry concerning this communication or earlier communications from the examiner should be directed to ANAND U. DESAI whose telephone number is (571)272-0947. The examiner can normally be reached on Monday - Friday 9:00 a.m. - 5:30 p.m.

If attempts to reach the examiner by telephone are unsuccessful, the examiner's supervisor, Andrew J. Wang can be reached on (571)272-0811. The fax phone number for the organization where this application or proceeding is assigned is 571-273-8300.

Information regarding the status of an application may be obtained from the Patent Application Information Retrieval (PAIR) system. Status information for published applications may be obtained from either Private PAIR or Public PAIR. Status information for unpublished applications is available through Private PAIR only. For more information about the PAIR system, see http://pair-direct.uspto.gov. Should you have questions on access to the Private PAIR system, contact the Electronic Business Center (EBC) at 866-217-9197 (toll-free). If you would like assistance from a USPTO Customer Service Representative or access to the automated information system, call 800-786-9199 (IN USA OR CANADA) or 571-272-1000.

November 7, 2009
/ANAND U DESAI/
Primary Examiner, Art Unit 1656